REMARKS

The Office Action mailed April 19, 2005 set an initial three (3) month period for response. Accordingly, a timely response without extension of time is presently due July 19, 2005.

Applicants thank Examiner Venci, and his supervisor, Lang Le, for their courtesy in a telephonic interview held May 25, 2005. Applicants have reviewed the Examiner's Interview Summary mailed June 23, 2005. Applicants will submit Applicants' Interview Summary under separate cover.

Claims 1, 4, 5, 6, 10, 11 and 12 have been amended to more particularly point out and distinctly claim methods of Applicants' invention and correct some minor errors. Withdrawn claims 22, 32 and 34 have also been amended. Applicants submit that these amendments are clearly supported by the specification and claims as filed and give rise to no issue of new matter. Applicants submit that these amendments put the claims in better form for consideration on appeal and to clarify issues for appeal and, therefore, are properly presented at this time and are enterable (See, e.g., 37 C.F.R. § 1.116(b)). Applicants request that these amendments be entered.

The Restriction Requirement

Applicants note that the Examiner has made his Restriction Requirement final.

Applicants reiterate their traverse made in the Amendment filed January 6, 2005 and note the following. Independent claims 1 and 6 are directed to methods for quantification of amount of a glycated form of a selected protein relative to total amount of the selected protein (glycated and non-glycated forms) in a biological sample using measurement of a selected property of the selected protein. Applicants note that independent claim 22 (considered to be withdrawn by the Examiner as directed to a non-elected invention) is directed to methods of quantitation of a glycated form of a selected non-hemoglobin protein relative to total amount of the selected protein (glycated and non-glycated forms) in a biological sample wherein the selected protein is optionally labeled with a specific selected protein label. Claim 22 further specifies steps of making optical measurements at a wavelength at which either the selected protein or the specific selected protein binding agent absorbs light. Applicants submit that binding of a specified selected protein binding agent by the selected protein is a selected property of the selected

protein (see claims 1 and 6). Accordingly, the subject matter of withdrawn claim 22 (and those claims dependent on it) may be properly examined with that of elected claims 1 to 21 without undue burden on the Examiner. Applicants request that the Examiner reconsider his position on the restriction requirement for claims 22 to 34 and withdraw it.

The Section 112, First Paragraph Rejection of Page 3

Claim 1 stands rejected under 35 U.S.C. § 112, first paragraph as assertedly failing to comply with the written description requirement. In particular, the Examiner appears to object to the terms "form" and "forms" when applied to a protein to be quantitated.

This rejection is respectfully traversed. Applicants submit that the claims, as pending after entry of the present amendments, clearly comply with the written description requirement of the first paragraph of Section 112.

Applicants note that it is well known to those of skill in the art that certain proteins inherently exist in multiple forms. Accordingly, there is no need to affirmatively recite that such protein(s) exist in one or more forms. For example, it is known that hemoglobin and albumin exist in multiple forms, including glycated and non-glycated forms. Accordingly, Applicants submit that their use of the terms "form" and "forms" are clearly embraced within the disclosure of the specification and claims as originally filed.

The Section 112, First Paragraph Rejection of Pages 3 to 6

Claims 1 to 21 stand rejected under 35 U.S.C. § 112, second paragraph as asserted indefinite.

The Examiner appears to object to certain terms. This rejection is respectfully traversed.

As noted hereinabove, independent claims 1, 6 and 12 have been amended to more particularly point out and distinctly claim methods of Applicants' invention.

Applicants note that the Examiner appears to object to certain terms as assertedly indefinite. Applicants note that the meaning of such terms, as used in the context of the claims as presently pending, would be understood by one of skill in the art. For example, Applicants submit that terms such as "negatively charged group" and "forms" are well known to those of skill in the art and their meanings, when read in the context of the present claims, would be

understood. Thus, Applicants submit that use of such terms complies with the second paragraph of Section 112.

Applicants submit that the claims as pending after entry of the present amendments clearly comply with the requisites of the second paragraph of Section 112. Applicants request that the Examiner reconsider this rejection in view of the claims as presently pending and withdraw it.

The Section 102(b) Rejection over Dean et al.

Claims 1 to 4 stand rejected under 35 U.S.C. §102(b) as anticipated by United States Patent No. 4,269,605 to Dean et al. ("Dean et al.").

Applicants note that in order to anticipate a claim or claims, a single reference must teach every element of the claim or claims. Applicants submit that Dean et al. clearly do not teach every element of any of claims 1 to 4.

In particular, Applicants submit that Dean et al. do not anticipate independent claim 1. Dean et al. describe a method which is different from that of Applicants' claim 1 and which lacks all of the elements of claim 1. Dean et al. is directed to a method for separating glycated protein from other proteins by forming a complex between glycated protein and a dihydroxyboryl reactive agent, and separation of non-glycated protein from glycated protein-dihydroxyboryl complex by washing. The non-glycated protein does not bind to the dihydroxy boryl agent.

In contrast, Applicants' claim 1 is directed to a method of quantitating relative amount of a glycated form of a selected protein relative to total amount of the selected protein (glycated and non-glycated forms) in a biological sample where a sample suspected of having both glycated and non-glycated forms of the selected protein to be quantitated is contacted with a solid support matrix under conditions where both the glycated and non-glycated forms of the selected protein bind to the solid support matrix. The matrix is washed with a first buffer to remove protein which does not bind under those conditions. The solid support matrix is then contacted with a second buffer at a pH where the glycated form of the selected protein binds to the solid support matrix, but where the non-glycated form of the selected protein does not substantially bind to the matrix, using an amount of the second buffer sufficient to rinse off the non-glycated form of the selected protein from the solid support matrix.

Applicants note that Dean et al. fail to teach a step where the solid support matrix is treated under conditions where both glycated and non-glycated forms of a selected protein bind to the solid support matrix, followed by a step where the matrix is treated under conditions where the glycated form of the selected protein binds and non-glycated forms do not substantially bind. Applicants submit that the Examiner's assertion that "Dean et al. nevertheless inherently teach this step" (Office Action mailed April 19, 2005 at page 12) is incorrect. This assertion appears to be related to the Examiner's comments regarding "eluted." With respect to the Examiner's comment regarding "eluted", Applicants submit that the Examiner is mistaken in what Dean et al. describe. Applicants submit that Dean et al.'s use of "eluted" at col. 5, lines 11 to 12 does not teach that the non-glycated form is in fact bound to a column and then washed off. Dean et al. teaches that binding of the non-glycated form is negligible. (See, Col. 8, lines 10 to 11).

Applicants submit that in view of the failure of Dean et al. to teach steps (a) to (c) of claim 1, Dean et al. do not anticipate claim 1. Claims 2 to 4 are dependent on claim 1 and incorporate additional elements. In view of the failure of Dean et al. to teach all the elements of claim 1, claims 2 to 4 which include additional elements, cannot be anticipated by Dean et al. Accordingly, these claims are also not anticipated.

The Section 103(a) Rejection over Dean et al. in view of Sanders and May & Richards

Claims 6 to 10 and 12 to 21 stand rejected under 35 U.S.C. §103(a) as unpatentable over Dean et al. in view of United States Patent No. 4,407,961 to Sanders ("Sanders") and published UK Application No. 2 206 411 to May & Richards ("May & Richards").

This rejection is respectfully traversed.

Independent claim 6 is directed to a method of quantitation of amount of a glycated form of a selected protein relative to the total amount of the selected protein (non-glycated and glycated forms). Claims 7 to 10 are dependent or ultimately dependent on claim 6.

Independent claim 12 is directed to a method of quantitation of amount of a glycated form of hemoglobin relative to total amount of hemoglobin (glycated and non-glycated forms) in a biological sample using an optical reading to determine amount of hemoglobin. Claims 13 to 21 are dependent or ultimately dependent on claim 12.

Applicants note their comments made hereinabove with regard to Dean et al. Applicants note that the Examiner admits that "Dean et al. do not teach the claimed first buffer pH 5.0 to 7.9

range for binding glycated and non-glycated protein to a negatively charged ion-exchange matrix" (see page 8 of the Office Action mailed April 19, 2005).

In making the present rejection, the Examiner asserted that Sanders taught a buffer having a pH of 6.4 to 7.2 for binding protein to a solid support matrix having a negative charge citing Sanders at Co. 2, line 35. (See, Office Action mailed April 19, 2005 at page 8.) Applicants submit that this assertion of the Examiner regarding what Sanders teaches is incorrect. Applicants note that, in fact, Sanders teaches use of such a buffer for "selectively binding non-glycosylated hemoglobin" (see Col. 2, lines 32 to 33) and furthermore notes that such a solid support-buffer system "causes binding of non-glysosylated hemoglobin without binding of glycosylated hemoglobin" (Col. 2, lines 46 to 52). Accordingly, Applicants submit that clearly Sanders neither teaches nor suggests a buffer in the pH 5.0 to 7.0 range that binds both glycosylated and non-glycosylated forms of hemoglobin.

Also, in making the present rejection, the Examiner asserted that May & Richards teach a method of quantitation of glycated protein using both a negatively charged group and a hydroxyboryl compound. Applicants note that May & Richards appear to teach an assay device incorporating two distinct zones through an eluted sample passes. The first zone is said to be capable of binding only glycated hemoglobin and the second zone is said to be capable of binding all residual hemoglobin that passed through the first zone. (See, e.g., page 2). May & Richards teach that after being applied, the sample moves through the first zone and then the second zone. Applicants note further that May & Richards teaches that the hydroxyboryl compound is in zone 1 and the support having a negatively charged group is in zone 2. May & Richards do not suggest either a solid support matrix comprising both a negatively charged group and a hydroxyboryl group or combining the groups they teach for zone 1 and zone 2 in the same zone.

Thus, Applicants submit that the combination of Sanders and May & Richards with Dean et al. clearly do not cure the deficiencies of what Dean et al. would fairly teach or suggest to one of skill in the art so as to render claims 6 to 10 and 12 to 22 obvious.

Applicants request that the Examiner reconsider the rejection in view of these remarks and withdraw it.

The Section 103(a) rejection over Dean et al. in View of Goldstein et al.

Claim 5 stands rejected over Dean et al. in view of Goldstein et al., 20 Diabetes Care S-18 (1947) ("Goldstein et al.").

This rejection is respectfully traversed. Applicants submit that Dean et al., when taken in view of Goldstein et al., do not suggest nor make obvious claim 5.

Claim 5 is dependent on claim 3 (which is dependent on claim 1) and specifies that the selected protein is albumin. As Applicants noted above, Dean et al. do not anticipate or make obvious claim 3. With respect to claim 5, the Examiner asserts that Goldstein et al. are said to teach that detection of glycated albumin would be a useful test for glycemia in diabetes. Assuming arguendo that the Examiner's assertion regarding Goldstein is correct, Goldstein et al. do not cure the deficiencies of what Dean et al. fairly teach or suggest to one of skill in the art (as applicants have noted hereinabove).

Applicants submit that the combination of Goldstein et al. with Dean et al. does not render claim 5 obvious.

The Section 103(a) Rejection over Dean et al. in view of Sanders, May & Richards and Goldstein et al.

Claim 11 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Dean et al., in view of Sanders, May & Richards and Goldstein et al.

This rejection is respectfully traversed. Applicants submit that Dean et al. taken in view of Sanders, May & Richards and Goldstein et al. neither suggest nor make obvious claim 11.

Claim 11 is dependent on claim 9 (which is ultimately dependent on claim 6). Claim 11 specifies that the selected protein is albumin.

Applicants direct the Examiner's attention to their remarks regarding what the cited references fairly teach or suggest to one of skill in the art as set forth hereinabove.

As Applicants previously noted, Dean et al. in view of Sanders and May & Richards neither suggest nor make obvious claims 6, 7, 8 or 9. Applicants note that claims 6 to 9 do not specify the selected protein. Applicants note that Goldstein et al. at most appear to suggest that measurement of glycated albumin may be useful for monitoring glycemic status in diabetic patients. With regard to the claimed quantitation method of claim 11, Applicants submit that

Goldstein et al. do not provide guidance for curing the deficiencies of what Dean et al., taken in view of Sanders and May & Richards would fairly teach or suggest. Accordingly, the further combination of Goldstein et al. with Dean et al., taken in view of Sanders, May & Richards and Goldstein et al. clearly does not make claim 11 obvious.

Applicants request that the Examiner reconsider this rejection and withdraw it.

CONCLUSION

In view of the foregoing, Applicants submit that claims 1 to 21 are allowable. Applicants request that claims 22 to 34 be rejoined for examination and prosecution. Applicants submit that those claims include allowable subject matter. Applicants request that the claims be allowed and passed to issue.

If the Examiner believes that a telephonic interview would expedite prosecution of this Application, he is encouraged to telephone the undersigned Applicant's attorney.

Please charge any fees associated with the submission of this paper to Deposit Account Number 50-2212. The Commissioner for Patents is also authorized to credit any over payments to the above-referenced Deposit Account.

Respectfully submitted,

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